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ACT Wrap Up

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Animal Health

ALEXANDRA BECKSTETT, STEPHANIE L. CHURCH, AND ERICA LARSON

Kentucky is home to some of the country's most famous breeding farms and, for good reason, boasts many top-class equine reproduction specialists. Earlier this year, the commonwealth also played host to the 2013 American College of Theriogenology (ACT) Symposia and Conference, which took place Aug. 7-10 in Louisville. Attendees from around the country with an interest in equine reproduction listened to lectures from top veterinarians on a variety of topics, including foal care, mare reproductive problems, stallion management, and more. Here are just a few highlights from the comprehensive equine sessions at this year's ACT Conference. For more articles from the event, visit TheHorse.com/ACT2013.

Pain's Impact on Reproduction

A broodmare battling chronic laminitis, a stallion with recurrent uveitis, and a maiden mare with persistent tendinitis: While these horses and their conditions are each distinct, the animals do share the potential for pain-related fertility problems.

L. Chris Sanchez, DVM, PhD, Dipl. ACVIM, an associate professor and director of the University of Florida's Hofmann Equine Neonatal ICU, admitted equine researchers don't know much about the pain-fertility relationship, but she pointed out that "the whole horse affects reproduction ... external environment can affect whatever body system you're dealing with."

What makes equine pain especially

problematic is the simple fact that horses can't describe it. "In people, pain is self-reported," she said, meaning it is what the patient says it is. "In animals and nonverbal humans, pain assessment is always based on the perception of an observer, be that an owner, trainer, or veterinarian."

Citing a clear correlation between lameness and fertility in cattle, she said there's something to be learned from what researchers have determined in looking at other species. She said humans and pigs have higher pain thresholds during late gestation in labor that reverse postpartum, which could be due to hormones causing opioid effects (based on research in sows).

Looking to dairy cattle, veterinarians have seen inversely proportional relationships between pain and fertility; lameness has had a substantial impact on dairy cows' welfare and the producers' bottom line (research based on a Florida study of claw lesions). Sanchez reviewed a few other findings, in which lame cows:

- Had a lower pregnancy rate after first insemination after calving;
- Had lower body condition scores during estrus, as well as lower social status and decreased estrous behavior;
- Had increased numbers of ovarian cysts;
- Achieved low conception at first service, showed a lack of ovarian activity, and experienced an increased time to conception; and
- May have had decreased sexual or "stress-related" pheromones or decreased ability to process them.

Even though cattle are ruminants and not bred to perform as athletes, "There's no reason to assume (pain's effect on reproduction is) different in horses," Sanchez said.

Moving on to pain management, Sanchez ran down the list of options and combinations veterinarians generally use. Practitioners select analgesics (painkillers) for each of their painful patients based on personal experience and what they learn from emerging studies and information. "It's important to remember that drugs work differently in different species, so the best pain killer for people or dogs is not necessarily the best option for horses, and vice versa," she explained. "Horses with extremely painful conditions, such as severe laminitis, may require a constant IV (intravenous) infusion of one or more medications to relieve pain."

Sanchez described some of the pros and

MYCOTOXIN ZEARALENONE'S EFFECTS ON MARE FERTILITY

Most breeders are familiar with the potentially dangerous effects of grazing broodmares on pasture containing endophyte-infected tall fescue: agalactia (poor milk let-down), dystocia (difficulty foaling), thickened placenta ("red bag" foal), and even foals that are born weak or dead.

But veterinarians know less about another potentially toxic substance that could be lurking in broodmares' feed: a mycotoxin called zearalenone. Heath King, DVM, Dipl. ACT, an assistant clinical professor at the Mississippi State University College of Veterinary Medicine, presented a poster chronicling recent research on zearalenone's effects on mares' reproductive performance.

Researchers know that zearalenone—primarily produced by the mold *Fusarium graminearum* and commonly found in barley, oats, wheat, corn, silage, rice sorghum, and some forages—has estrogenic effects (causes estrus) in swine and causes reproductive problems in cattle. However, its effects on equine reproduction remain relatively unknown, King said. So he and colleagues set out to evaluate the reproductive efficacy of healthy mares consuming two different zearalenone concentrations daily.

The team separated 21 mature, reproductively healthy mares into three groups of seven. One group served as a control and consumed one-half kilogram of pelleted feed daily; horses in another consumed 2 milligrams (mg) of zearalenone in addition to the pelleted feed (the "low-dose" group); and the remaining horses consumed 8 mg of zearalenone daily in addition to the pellets (the "high-dose" group). The mares began treatment on a day they ovulated, and the study continued for three subsequent estrous cycles. The researchers monitored the mares' reproductive activity throughout the study, and mares were bred during their third estrus.

Key findings included:

- The average interovulatory interval (the number of days between ovulation) was 20.3 days for control mares, 21.5 days for low-dose mares, and 21.1 days for high-dose mares.
- Pregnancy rates were 6/6 in controls, 3/6 in low-dose mares, and 7/7 in high-dose mares. These pregnancy rates did not differ significantly from one another in a pairwise comparison.
- Mean serum concentrations of the hormones estradiol and progesterone did not differ significantly between groups on the sampled days.

King and colleagues determined that these initial results indicated zearalenone did not cause any adverse reproductive effects when consumed in low, "environmentally relevant" doses.

—Erica Larson



A potentially toxic substance could be lurking in your broodmare's feed.

THE HORSE STAFF

cons of each drug class, some of the combinations that seem to work best, as well as which ones appear most likely to cause more harm or little good.

Most drugs currently available to treat pain in horses have the potential for adverse effects, she said, primarily associated with the gastrointestinal tract or kidneys. It's also important to recognize that numerous drugs can work differently in healthy horses versus painful horses and pain itself can have many of the same effects. So, no matter the analgesic of choice, efficient response to pain is the best approach. "It's a pay now or pay later kind of situation," she explained. "Decrease windup by getting

pain under control early."

Sanchez summarized that with few existing research studies on equine pain, "It is not particularly surprising that an association between pain and fertility—or infertility—has not been established in the horse. The lack of data, however, certainly does not infer lack of relationship."

Do Equine Metabolic Diseases Affect Reproductive Ability?

Having trouble getting your mare pregnant? It might be time to take a good look at her weight and metabolic condition. Some veterinarians now believe metabolic diseases negatively impact reproduction.

Peter Morresey, BVSc, MACVSc, Dipl. ACT, ACVIM, an associate at Rood & Riddle Equine Hospital, in Lexington, Ky., said much of what veterinarians know about reproduction-related metabolic disorders in horses comes from human medicine and research in other species. But is there a parallel between metabolic issues known to cause problems in human reproduction and those in horses? It's possible.

Veterinarians already know that metabolic syndrome in mares can negatively affect insulinlike growth factors, which are key to ovarian follicle selection (for maturing and subsequent egg release). These effects might ultimately impair ovarian function.

Additionally, he said, obesity has been shown to prolong both estrous duration—leading to fewer usable breeding cycles each year—and ovulatory activity during the nonbreeding season. And while researchers have shown that a drug called metformin can help obese horses shed pounds and return their body systems closer to normal, Morresey said it has not been uniformly effective in helping resolve obese mares' reproductive issues.

Another concern, he said, is gestational insulin resistance. All mares become insulin resistant during late pregnancy (generally after about 270 days), and if they consume high-starch feeds they exhibit exaggerated insulin and glycemic responses, whereas mares consuming a fat- and fiber-based diet show less exaggerated responses. The negative effects might be amplified in mares already insulin-resistant going into pregnancy, he said.

So how should owners and veterinarians manage breeding horses with confirmed or suspected metabolic disease? First, make a good diagnosis. Morresey cautioned that researchers have shown that none of the available antemortem (conducted in the live horse) diagnostic tests are completely reliable. Rather, he encouraged practitioners to rely on clinical impressions during the physical exam, including watching for abnormal fat distribution on the horse's body—especially in front of the mammary glands and sheath—and for other tell-tale signs (e.g., hoof ridges) of metabolic disease. He also cautioned that fat in the nuchal ligament (in the neck, which forms the "cresty" neck) has been proven to have higher levels of pro-inflammatory cytokines (mediators of inflammation) than fat in other locations.

Morresey implements a multifaceted treatment approach in confirmed cases:

Dietary control First, veterinarians might need to help an owner recognize and accept that his or her horse needs to lose weight. Once everyone is on the same page, remove concentrates from the horse's diet, limit pasture access (either through a drylot or using a grazing muzzle), provide hay at a rate of 1-1.25% of body weight, and divide the horse's rations into several small

feedings throughout the day.

Exercise A horse that is foot sore or reluctant to move can be challenging to exercise but, despite conflicting study results on whether exercise improves insulin sensitivity, Morresey said it's often in the horse's best interest to get moving.

Pharmacologic aids There are several different drugs that might help get metabolic horses back on track, he said. Clinically, veterinarians have found success using



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metformin to help horses by decreasing the liver's glucose production, increasing peripheral absorption of glucose by cells, and decreasing glucose absorption in the gut (these are the proven human mechanisms, he said); however, he noted that the drug hasn't always performed well in equine research settings. Another medication, L-thyroxine, can increase insulin sensitivity in horses; Morressey noted that if he had to choose a sole medication for a metabolic horse, he'd likely select L-thyroxine. Additionally, if a veterinarian is treating a mare with confirmed or suspected Cushing's disease, he recommended putting her on pergolide, despite one of the drug's side effects being agalactia (absence of colostrum and milk production).

"You can get colostrum from another source," he said, adding that in clinical practice, he and others have successfully "maintained pregnant mares on pergolide throughout gestation when dictated by the health of the mare without detriment to foal delivery or adequate milk production."

Researchers are making strides in understanding how metabolic disease impacts reproduction, but much is still a mystery. However, evidence suggests that metabolic diseases could negatively affect equine reproduction.

Oviduct Issues in Mares

Anomalies of the slender channel through which eggs travel from ovary to uterus rarely impact fertility, but it's important breeders are aware of what can be a problem and what usually isn't. Patricia Sertich, VMD, Dipl. ACT, associate professor at the University of Pennsylvania's School of Veterinary Medicine, reviewed common equine oviductal anomalies.

Hydatid of Morgagni Commonly called fimbrial cysts, Sertich said hydatid of Morgagni is a standard anomaly found in the equine oviduct and is generally located on the cranial edge (that closest to the horse's skull) of the infundibulum (the structure that coaxes the oocyte into the oviduct). These cysts are typically incidental (secondary and relatively unimportant) findings, and small cysts generally do not require treatment, but larger cysts could interfere with oocyte transport. These larger cysts are easily removed with a laser, she said.

Mesonephric Duct Remnants Sertich said veterinarians frequently identify cystic remnants of the mesonephric duct (an organ present during embryogenesis, the

COULD INTRAUTERINE MARBLES CAUSE PYOMETRA IN MARES?

One method of controlling mares' estrous cycles and reducing estrus-related behavior involves placing a marble in the mare's uterus, which essentially keeps her from cycling. While veterinarians have noted no significant uterine problems during treatment with this technique in the past, Jessica Klabnik-Bradford, a veterinary student at the Kansas State University (K State) College of Veterinary Medicine; Maria Soledad Ferrer, DVM, MS, Dipl. ACT, clinical associate professor of theriogenology at K State; and a team of veterinarians from the college recently encountered what they believe to be a significant complication.

A 16-year-old Appaloosa mare with no reproductive history presented to K State with a foul-smelling suppurative (pus-producing) vulvar discharge, Klabnik-Bradford said. On ultrasonographic exam, veterinarians found a corpus luteum (the structure formed after the ovarian follicle releases the egg and then produces progesterone) and a 34-millimeter round structure in the left uterine horn. The team confirmed pyometra (infection of the uterus) and suspected that the structure was either a mummified fetus or an intrauterine marble.

Uterine endoscopy confirmed the latter, and they removed the marble from the mare's uterus.

"After questioning the owners, it was determined that the marble had been in place for at least two years," Klabnik-Bradford said. "This case suggests that pyometra may be a complication of using intrauterine marbles for estrus suppression in mares and stresses the importance of removing the marble once estrus suppression is no longer desired."

Both Klabnik-Bradford and Ferrer recommended that only veterinarians skilled in equine reproduction place intrauterine marbles for estrus suppression.

"Since the marble acts by prolonging function of the corpus luteum, the treatment will not be effective in mares in winter anestrus or spring transition that are not ovulating and producing corpora lutea," Ferrer added. "Therefore, removal of the marble during winter may be recommended."—Erica Larson



Veterinarians encountered a potential intrauterine marble complication.

COURTESY DR. KLABNIK-BRADFORD

process by which the embryo forms and develops, which eventually becomes part of male reproductive organs) in pregnant mares, but they are not thought to contribute to infertility.

Adhesions Veterinarians find oviductal adhesions—thin strands of fibrous tissue stretching from the infundibulum to the ovary—incidentally when examining mares postmortem that have had many foals, Sertich said. Less commonly they find thicker adhesions (more than 4 millimeters thick). "Although the etiology is not completely understood, the thin strands are often seen with blood clots and may be associated with ovulation," Sertich explained. "The thicker strands have not been seen to be associated with blood clots."

Hydrosalpinx Sertich said hydrosalpinx—a disorder in which the oviduct is blocked and filled with a watery, clear liquid—is rare in mares. While the disorder can negatively impact fertility, it doesn't necessarily prevent mares from producing offspring.

Sertich also noted that, providing the uterus is healthy, a mare with hydrosalpinx could likely carry a foal to term if she acted as an embryo transfer recipient.

Salpingitis An infection or inflammation of the oviduct, salpingitis is not a common cause of infertility in mares, Sertich said.

Globular Masses These noncellular masses are most common in mares aged 7 and older and are commonly found in the oviductal lumen (cavity). The epithelium surrounding them is generally healthy and intact. Globular masses generally aren't associated with infertility.

"Considering that significant abnormalities of the oviduct are not common and since the diagnostic tests are time-consuming, possibly inconclusive, invasive, and not without risk to the mare, it is recommended that a thorough evaluation of the mare's genital tract and management be made before pursuing specific oviductal tests and treatments," Sertich concluded.

Equine Placentitis Update

Placentitis—an inflammation of the placenta—is often caused by an ascending infection, which means it enters the mare's uterus through the cervix. C. Scott Bailey, DVM, MS, Dipl. ACT, an assistant professor of theriogenology at the North Carolina State University (NCSU) College of Veterinary Medicine, explained that placentitis is responsible for 10-40% of late-term abortions in mares; of those cases 60% are caused by the bacterial variety.

While catching cases early would likely improve the chances of positive clinical outcomes, veterinarians are currently limited in their diagnostic options for placentitis. Still, Bailey brought veterinarians up to date on the latest information on diagnosing and treating the condition.



COURTESY/DR. PATRICIA SERTICH

Oviductal adhesions are strands of fibrous tissue stretching from the infundibulum to the ovary.

Ultrasound screening Ultrasound examination of the uterus and placenta is the mainstay of placentitis diagnostics. Bailey said measurements greater than the normal combined thickness of uterus and placenta (CTUP) for healthy pregnant mares—often referred to as “early thickening”—are clear indicators of uterine pathology and suggestive of placentitis.

The challenge? “Frequent monitoring of mares with no known risk factors for placentitis represents a significant expense and may not be cost-effective or feasible,” Bailey said. Nonetheless, he noted this technique is the most sensitive and specific diagnostic and screening tool he can recommend for valuable or high-risk patients.

Hormone tests Bailey said researchers have also explored the efficacy of measuring serum progesterone to diagnose or screen for placentitis. In mares with compromised pregnancies, he said, previous research has shown that serum progesterone levels either elevate prematurely or drop severely.

“Prematurely rising progesteragens are indicative of chronic stress to the foal,” he said, noting that placentitis is the most common cause of fetal stress. “Falling progesteragens indicate fetal demise and are not specific. Elevated progesteragen may occur at the same time as early thickening. Usually if progesteragens are dropping quickly, treatment is too late.”

SAA tests Bailey described recent work in which researchers explored using inflam-

matory blood protein levels to identify inflammation within the body. Specifically, researchers tried identifying mares with experimentally induced placentitis in late gestation by measuring levels of an inflammatory protein called serum amyloid A, or SAA. They found that mares' serum SAA levels rose significantly 48-144 hours after experimental infection, while control mares' SAA levels remained low.

“These findings warrant further work in

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clinical cases of naturally occurring placentitis to determine whether SAA may be used as an inexpensive, sensitive screening tool for placental function, and whether it is influenced by confounding factors such as extra-uterine disease (not having to do with the uterus) or obesity,” Bailey said.

He cautioned that any inflammation or infection within the body can cause SAA levels to rise, so veterinarians should interpret such results with caution.

Traditionally, veterinarians have used a combination of anti-inflammatory drugs, antibiotics, immunomodulatory medications, and progestins to treat placentitis. Bailey described a study in which investigators treated experimentally infected mares with a combination of trimethoprim sulfamethoxazole (TMS, a commonly used antibiotic), pentoxifylline (a common anti-inflammatory drug), and altrenogest (ALT, a common progestin), and

recorded good results: 83% of those mares delivered viable foals, whereas no viable foals were born in the control group. Unfortunately veterinarians haven’t had the same results when treating mares in clinical practice.

Additionally, he said, researchers from his laboratory showed that delaying placentitis treatment until CTUP measurements increased resulted in only 40% of mares delivering viable foals. Thus, he stressed the importance of contacting a veterinarian at the first signs of placentitis, such as unusual mammary development or vaginal discharge.

Bailey also reviewed some research regarding the different placentitis therapeutic options:

“Frequent monitoring of mares with no known risk factors for placentitis represents a significant expense and may not be cost-effective or feasible.”

DR. C. SCOTT BAILEY

Antibiotics Bailey said some of the common antibiotic agents veterinarians use to treat placentitis include TMS, cephalosporins, tetracyclines, sulfonamides, carboxypenicillins, and penicillin plus betalactamase inhibitors, all of which have been proven effective in controlling placentitis-causing bacteria *in vitro* (in the laboratory). He noted that researchers have learned much about the different drugs over the years:

- Gentamicin, penicillin G (another antibiotic drug), and TMS can all reach therapeutic concentrations in allantoic fluid (fluid in the outer layer of the placenta where the placenta and maternal uterus touch and exchange nutrients);
- Penicillins are “highly effective” against *Streptococcus zooepidemicus*, one of the common bacteria found in mares with placentitis;
- Gentamicin is effective against most of the Gram-negative bacteria that cause placentitis; and
- Although TMS performs well in *in vitro*

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trials, the medication wasn't able to clear *S. zooepidemicus* from experimentally infected mares' uteri.

"Hospitalized patients are generally treated with a combination of standard doses of penicillin G and gentamicin," Bailey said. "However, the need for repeated drug administration and catheter maintenance makes this combination impractical for prolonged therapy of patients maintained in a farm setting, (so instead) TMS is widely used for this purpose."

Anti-inflammatory drugs Bailey said vets often use flunixin meglumine (marketed as Banamine, a non-steroidal anti-inflammatory drug) to treat placentitis, as previous research suggests it could help improve foal viability. In another study researchers showed it can help prevent prostaglandin synthesis and luteolysis, two processes that can interrupt pregnancy.

Veterinarians might also use pentoxifylline to manage placentitis. While its mechanism of action isn't well-understood, Bailey said, it appears to help maximize the foal's chance of developing fully when used in combination with TMS and ALT.

Bailey said researchers are also taking a closer look at whether treating with glucocorticoids can improve fetal viability in mares with placentitis.

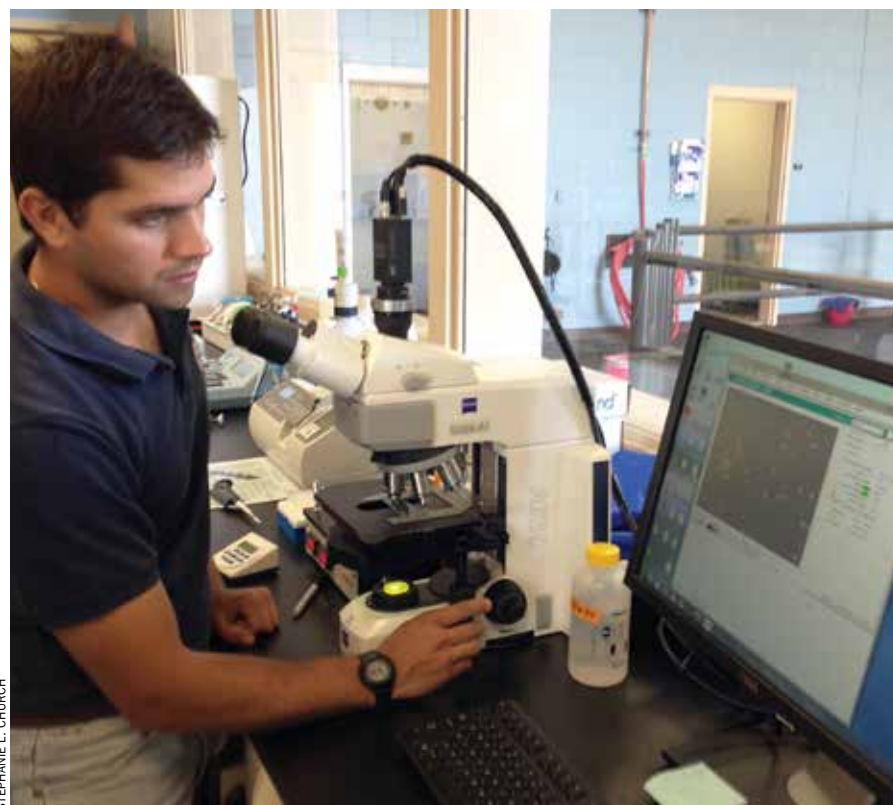
Bailey said that while researchers continue to examine placentitis, there are still many unanswered questions about the condition. In the meantime, Bailey stressed that early disease detection is a key to successful treatment, and he encouraged horse owners and managers to contact their veterinarians quickly if they notice signs of disease.

Stallion Semen Tests

Because breeding is a business, having a veterinarian evaluate your stallion's semen to determine his fertility (or lack thereof) is a key component of a breeding soundness examination. But semen evaluations are not always black and white, and there are many tests your veterinarian can perform. So Dickson Varner, DVM, Dipl. ACT, professor and Pin Oak Stud Chair of Stallion Reproductive Studies at Texas A&M University, walked attendees through the tests he uses to evaluate semen.

Although most haven't changed in recent years, Varner said tests were worth reviewing as there are many in use "that we might not be doing correctly, or the people we're overseeing at the farms aren't doing correctly."

The following are what he listed as important semen tests:



STEPHANIE L. CHURCH

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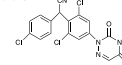
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For the treatment of equine protozoal myeloencephalitis (EPM) caused by *Sarcocystis neurona* in horses.

CAUTION
Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

NADA #141-288 Approved by FDA

DESCRIPTION
Diclazuril, (±)-2,6-dichloro-α-(4-chlorophenyl)-4-(4,5-dihydro-3,5-dioxo-1,2,4-triazin-2(3H)-yl)benzenesulfonamide, has a molecular formula of C₁₇H₁₀Cl₃N₄O₂, a molecular weight of 407.64, and a molecular structure as follows:



Diclazuril is an antiprotozoal (antiprotazol) compound with activity against several genera of the phylum Apicomplexa. PROTAZIL® (diclazuril) is supplied as oral pellets containing 1.56% diclazuril to be mixed as a top-dress in feed. Inert ingredients include dehydrated alfalfa meal, wheat middlings, cane molasses and propionic acid (preservative).

INDICATIONS

PROTAZIL® (1.56% diclazuril) Antiprotazol Pellets are indicated for the treatment of equine protozoal myeloencephalitis (EPM) caused by *Sarcocystis neurona* in horses.

DOSE AND ADMINISTRATION

Dosage: PROTAZIL® (1.56% diclazuril) is administered as a top dress in the horse's daily grain ration at a rate of 1 mg diclazuril per kg (0.45 mg diclazuril/lb) of body weight for 28 days. The quantity of PROTAZIL® necessary to deliver this dose is 64 mg pellets per kg (29 mg pellets/lb) of body weight.

Administration: To achieve this dose, weigh the horse (or use a weight tape). Scoop up PROTAZIL® to the level (cup mark) corresponding to the dose for the horse's body weight using the following chart:

Weight Range of Horse (lb)	mLs of Pellets	Weight Range of Horse (lb)	mLs of Pellets
275 - 524	20	1275 - 1524	60
525 - 774	30	1525 - 1774	70
775 - 1024	40	1775 - 2024	80
1025 - 1274	50		

One 2-lb bucket of PROTAZIL® will treat one 1100-lb horse for 28 days. One 10-lb bucket of PROTAZIL® will treat five 1100-lb horses for 28 days.

CONTRAINDICATIONS

Use of PROTAZIL® (1.56% diclazuril) Antiprotazol Pellets is contraindicated in horses with known hypersensitivity to diclazuril.

WARNINGS

For use in horses only. Do not use in horses intended for human consumption. Not for human use. Keep out of reach of children.

PRECAUTIONS

The safe use of PROTAZIL® (1.56% diclazuril) Antiprotazol Pellets in horses used for breeding purposes, during pregnancy, or in lactating mares has not been evaluated. The safety of PROTAZIL® (1.56% diclazuril) Antiprotazol Pellets with concomitant therapies in horses has not been evaluated.

ADVERSE REACTIONS

There were no adverse effects noted in the field study which could be ascribed to diclazuril.

To report suspected adverse reactions, to obtain a MSDS, or for technical assistance call 1-800-224-5318.

CLINICAL PHARMACOLOGY

The effectiveness of diclazuril in inhibiting merozoite production of *Sarcocystis neurona* and *S. falcatula* in bovine turbinate cell cultures was studied by Lindsay and Dubey (2001). Diclazuril inhibited merozoite production by more than 80% in cultures of *S. neurona* or *S. falcatula* treated with 0.1 mg/mL diclazuril and greater than 95% inhibition of merozoite production (IC₅₀) was observed when infected cultures were treated with 1.0 mg/mL diclazuril. The clinical relevance of the in vitro cell culture data has not been determined.

PHARMACOKINETICS IN THE HORSE

The oral bioavailability of diclazuril from the PROTAZIL® (1.56% diclazuril) Antiprotazol Pellets at a 5 mg/kg dose rate is approximately 5%. Related diclazuril concentrations in the cerebrospinal fluid (CSF) range between 1% and 5% of the concentrations observed in the plasma. Nevertheless, based upon equine pilot study data, CSF concentrations are expected to substantially exceed the in vitro IC₅₀ estimates for merozoite production (Dirlikov et al., 1999). Due to its long terminal elimination half-life in horses (approximately 43-65 hours), diclazuril accumulation occurs with once-daily dosing. Corresponding steady state blood levels are achieved by approximately Day 10 of administration.

EFFECTIVENESS

Two hundred and fourteen mares, stallions, and geldings of various breeds, ranging in age from 9 to 30 years, were enrolled in a multi-center field study. All horses were confirmed EPM-positive based on the results of clinical examinations and laboratory testing, including CSF Western Blot analyses. Horses were administered PROTAZIL® (1.56% diclazuril) Antiprotazol Pellets at doses of 1, 5, or 10 mg diclazuril/kg body weight as a top-dress on their daily grain ration for 28 days. The horses were then evaluated for clinical changes via a modified Mayhew neurological scale on Day 48 as follows:

- Normal, neurological deficits not detected.
- Neurological deficits may be detectable at normal gaits; signs exacerbated with manipulative procedures (e.g., backing, turning in tight circles, walking with head elevation, truncal swaying, etc.).
- Neurological deficit obvious at normal gaits or posture; signs exacerbated with manipulative procedures.
- Neurological deficit very prominent at normal gaits; horses give the impression they may fall (but do not) or buckle or fall with manipulative procedures.
- Neurological deficit is profound at normal gait; horse frequently stumbles or trips and may fall at normal gaits or when manipulative procedures were utilized.
- Horse is recumbent, unable to rise.

Each horse's response to treatment was compared to its pre-treatment values. Successful response to treatment was defined as clinical improvement of at least one grade by Day 48 ± conversion of CSF to Western Blot-negative status for *S. neurona* or achievement of Western Blot-negative CSF status without improvement of 1 ataxia grade.

Forty-two horses were initially evaluated for effectiveness and 214 horses were evaluated for safety. Clinical condition was evaluated by the clinical investigator's subjective scoring and then corroborated by evaluation of the neurological examination videotapes by a masked panel of three equine veterinarians. Although 42 horses were evaluated for clinical effectiveness, corroboration of clinical effectiveness via videotape evaluation was not possible for one horse due to missing neurologic examination videotapes. Therefore, this horse was not included in the success rate calculation.

Based on the numbers of horses that seroconverted to negative Western Blot status, and the numbers of horses classified as successes by the clinical investigators, 28 of 42 horses (67%) at 1 mg/kg were considered successes. With regard to independent expert masked videotape assessments, 10 of 24 horses (42%) at 1 mg/kg were considered successes. There was no clinical difference in effectiveness among the 1, 5, and 10 mg/kg treatment group results.

Adverse events were reported for two of the 214 horses evaluated for safety. In the first case, a horse was enrolled showing severe neurologic signs. Within 24 hours of dosing, the horse was recumbent, biling, and exhibiting signs of dementia. The horse died, and no cause of death was determined. In the second case, the horse began walking stiffly approximately 13 days after the start of dosing. The referring veterinarian reported that the horse had been fed grass clippings and possibly had laminitis.

ANIMAL SAFETY

PROTAZIL® (1.56% diclazuril) Antiprotazol Pellets were administered to 30 horses (15 males and 15 females, ranging from 5 to 9 months of age) in a target animal safety study. Five groups of 6 horses each (3 males and 3 females) received 0, 5 (5X), 15 (15X), 25 (25X) or 50 (50X) mg diclazuril/kg (2.27 mg/lb) body weight/day for 42 consecutive days as a top-dress on the grain ration of the horse. The variables measured during the study included: clinical and physical observations, body weights, food and water consumption, hematology, serum chemistry, urinalysis, fecal analysis, necropsy, organ weights, gross and histopathologic examinations. The safety of diclazuril top-dress administered to horses at 1 mg/kg once daily cannot be determined based solely on this study because of the lack of an adequate control group (control horses tested positive for the test drug in plasma and CSF). However, possible findings associated with the drug were limited to elevations in BUN, creatinine, and SDH and less than anticipated weight gain. Definitive test article-related effects were decreased grain/top-dress consumption in horses in the 50 mg/kg group.

In a second target animal safety study, PROTAZIL® (1.56% diclazuril) Antiprotazol Pellets were administered to 24 horses (12 males and 12 females, ranging from 2 to 8 years of age). Three groups of 4 horses/sex/group received 0, 1, or 5 mg diclazuril/kg body weight/day for 42 days as a top-dress on the grain ration of the horse. The variables measured during the study included physical examinations, body weights, food and water consumption, hematology, and serum chemistry. There were no test article-related findings seen during the study.

STORAGE INFORMATION

Store between 15°C to 30°C (59°F to 86°F).

HOW SUPPLIED

PROTAZIL® (1.56% diclazuril) Antiprotazol Pellets are supplied in 2-lb (0.9 kg) and 10-lb (4.5 kg) buckets.

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- Lindsay, D. S., and Dubey, J. P. 2000. Determination of the activity of diclazuril against *Sarcocystis neurona* and *Sarcocystis falcatula* in cell cultures. *J. Parasitology* 86(1):164-166.
- Dirlikov, L., Lehner, F., Natrass, E., Bentz, B. G., Woods, W. E., Carter, W. E., Karpiesak, W. G., Jacobs, J., Boyles, J., Harkins, J. D., Grandstrom, D. G., and Tobin, T. 1999. Diclazuril in the horse: Its identification and detection and preliminary pharmacokinetics. *J. Vet. Pharmacol. Therap.* 22:374-379.

May 2010

Intervet Inc.

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- Measurement of sperm numbers;
 - Sperm concentration;
 - Measuring semen volume;
 - Sperm motility;
 - Sperm morphology and abnormalities such as detached heads, coiled tails, premature germ cells, proximal droplets, and abnormal midpieces;
 - Sperm chromatin quality; and
 - Acrosomal integrity and function.
- Another important fertility measure-

ment is testicular size.

In summary, Varner advised veterinarians to be as thorough as possible when performing a breeding soundness examination on a stallion. A battery of laboratory tests will be more likely to help them predict stallion fertility than just a couple of tests.

For the complete article, including detailed descriptions of each test, see TheHorse.com/32535.

CEM Screening Techniques Tested

Researchers confirmed the importance of including exposed mares when conducting surveillance for contagious equine metritis (CEM) in the recent South African outbreak, along with specific stallion sampling and screening methods in that country for the venereal disease.

Catherine May, BVSc, and colleagues at the Veterinary Faculty of the University of Pretoria, recently completed two studies in the wake of a CEM outbreak in South Africa. They determined the carrier status of *Taylorella equigenitalis*—CEM's causative bacterium—among stallions and exposed mares and assessed the distribution of the agent on the stallions' external genitalia.

Screening for CEM cases and preventing its spread are important because the disease can cause temporary infertility in mares, said May, resulting in breeding losses and negatively impacting the economy when CEM-free countries ban imports from countries that have reported an outbreak. Though exposure to CEM doesn't impact a stallion pathologically, if his external genitalia are contaminated by *T. equigenitalis*, he can pass it to mares via natural cover breeding or through semen in assisted reproductive techniques. Mares that become infected, on the other hand, can show physical signs of infection, usually developing a vaginal discharge after breeding to a carrier stallion and/or returning to estrus quickly after breeding due to early embryonic death. Other mares might only be subclinically infected, meaning they show no signs of infection but have the ability to spread the bacterium.

The good news about CEM is that affected mares and stallions respond very well to treatment, although it may take more than one course of therapy to complete a full recovery; it's just a matter of identifying active cases and, more importantly, subclinical carriers.

"Traditionally, the disease has been considered as mainly a venereal or sexually transmitted disease, but research into the South African outbreak showed that fomite transmission (e.g., via breeding phantom and/or artificial vagina) may be even more important in the spread of this disease," May said. "Because most mares naturally rid themselves of the infection, and only a certain number of stallions become carriers, the actual extent of the outbreak will never be known." After the outbreak, researchers instituted a nationwide

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Top Reproduction Studies of 2012-13

Mary Beth Stanton, DVM, Dipl. ACT, of Equine Veterinary Reproduction Specialists, in Ocala, Fla., and Audrey Kelleman, DVM, Dipl. ACT, lecturer in large animal reproduction at the University of Florida College of Veterinary Medicine, each presented a handful of studies from 2012-13 that they found interesting and influential.

Colic Surgery and Pregnancy Outcome

In this retrospective study, researchers looked at the ability of the mares to carry a foal depending upon the gestational age at the time of colic surgery. “In a nutshell,” Kelleman said, “the prognosis for carrying a foal to term post-colic surgery was significantly better for those mares younger than 15 years of age and for those mares carrying pregnancies greater than 40 days gestation at the time of surgery.”

Stem Cell Delivery to the Uterus

“The object of this paper was to look at methods of stem cell delivery to ensure wide distribution in the uterus (to help treat endometrosis),” Stanton said. In study results, three of four affected mares that received stem cells via a method similar to that used for deep horn artificial insemination had positive staining for fluorescence of stem cell proliferation, indicating they were able to not only survive but also divide and develop.

“This could be a simple, noninvasive method of stem cell delivery resulting in a wide incorporation of stem cells,” Stanton concluded.

New Seminal Plasma Removal Method

In this study researchers compared the new “Sperm Filter” method of seminal plasma removal before freezing semen with the traditional method of centrifugation, which has the potential to cause mechanical damage to sperm. They found that they were able to recover more sperm from 31 stallions’ ejaculates using the filter than with centrifugation.

Embryo Transfer to Noncycling Mares

Stanton said the concept of this study was to use estradiol benzoate (the ester of a potent estrogen that prepares the uterus for implantation of the fertilized ovum) to prepare the mare’s uterus to expect an embryo. “This study aimed to prepare mares in anestrus (noncycling) or in the transitional period (between estrus and anestrus) as embryo recipients,” she said.

“Anestrus and transitional phase mares may be successfully prepared and impregnated (using this method) with comparable pregnancy rates to cycling mares,” Stanton concluded.

Uterine Torsion and Mare/Foal Survival

In this study researchers “looked at 12 pregnant mares between ages 3 and 12 that presented with colic signs, uterine torsion was confirmed on rectal palpation, and a midline celiotomy (surgical incision of the abdomen to correct torsion) was performed,” Stanton said.

The researchers concluded that “75% (9/12) of the mares survived, survival was poor closer to term, and the longer the duration of torsion the more compromised the mare and foal,” Stanton explained. “Seven of nine surviving mares were successfully rebred and went on to foal with no complications.”

Fertility and Survival Post-Cesarian Section

In this retrospective study researchers looked at mare and foal survival, as well as foaling rates subsequent to cesarean section. Mare survival to discharge was 84% and foal survival 34%. Foaling rate was lowest in the year following the surgery.

“Their conclusions were that foaling rates post-cesarean section were quite acceptable in cases where dystocia lasted less than 90 min (68% foaled) and in those mares younger than 16 years of age,” Kelleman said.

For more reproduction and foal-related studies from the past year, see TheHorse.com/32596 and TheHorse.com/32374.

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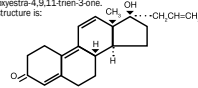


Regu-Mate® (altrenogest)

Solution 0.22% (2.2 mg/mL)

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: Regu-Mate® (altrenogest) Solution 0.22% contains the active synthetic progestin, altrenogest. The chemical name is 17 α -allyl-17 β -hydroxyestra-4,9,11-trien-3-one. The CAS Registry Number is 850-52-2. The chemical structure is:



Each mL of Regu-Mate® (altrenogest) Solution 0.22% contains 2.2 mg of altrenogest in an oil solution.

ACTIONS: Regu-Mate® (altrenogest) Solution 0.22% produces a progestational effect in mares.

INDICATIONS: Regu-Mate® (altrenogest) Solution 0.22% is indicated to suppress estrus in mares. Suppression of estrus allows for a predictable occurrence of estrus following drug withdrawal. This facilitates the attainment of regular cyclicity during the transition from winter anestrus to the physiological breeding season. Suppression of estrus will also facilitate management of prolonged estrus conditions. Suppression of estrus may be used to facilitate scheduled breeding during the physiological breeding season.

CONTRAINDICATIONS: Regu-Mate® (altrenogest) Solution 0.22% is contraindicated for use in mares having a previous or current history of uterine inflammation (i.e., acute, subacute, or chronic endometritis). Natural or synthetic gestagen therapy may exacerbate existing low-grade or “smoldering” uterine inflammation into a fulminating uterine infection in some instances.

PRECAUTIONS: Various synthetic progestins, including altrenogest, when administered to rats during the embryogenic stage of pregnancy at doses manyfold greater than the recommended equine dose caused fetal anomalies, specifically masculinization of the female genitalia.

DOSAGE AND ADMINISTRATION: While wearing protective gloves, remove shipping cap and seal; replace with enclosed plastic dispensing cap. Remove cover from bottle dispensing tip and connect luer lock syringe (without needle). Draw out appropriate volume of Regu-Mate solution. (Note: Do not remove syringe while bottle is inverted as spillage may result.) Detach syringe and administer solution orally at the rate of 4 mL per 110 pounds body weight (0.044 mg/kg) once daily for 15 consecutive days. Administer solution directly on the base of the mare’s tongue or on the mare’s usual grain ration. Replace cover on bottle dispensing tip to prevent leakage. Excessive use of a syringe may cause the syringe to stick; therefore, replace syringe as necessary.

WHICH MARES WILL RESPOND TO REGU-MATE® (altrenogest) SOLUTION 0.22%: Extensive clinical trials have demonstrated that estrus will be suppressed in approximately 95% of the mares within three days; however, the post-treatment response depended on the level of ovarian activity when treatment was initiated. Estrus in mares exhibiting regular estrus cycles during the breeding season will be suppressed during treatment; these mares return to estrus four to five days following treatment and continue to cycle normally. Mares in winter anestrus with small follicles continued in anestrus and failed to exhibit normal estrus following withdrawal. Response in mares in the transition phase between winter anestrus and the summer breeding season depended on the degree of follicular activity. Mares with inactive ovaries and small follicles failed to respond with normal cycles post-treatment, whereas a higher proportion of mares with ovarian follicles 20 mm or greater in diameter exhibited normal estrus cycles post-treatment. Regu-Mate® (altrenogest) Solution 0.22% was very effective for suppressing the prolonged estrus behavior frequently observed in mares during the transition period (February, March and April). In addition, a high proportion of these mares responded with regular estrus cycles post-treatment.

SPECIFIC USES FOR REGU-MATE® (altrenogest) SOLUTION 0.22%:

SUPPRESSION OF ESTRUS TO:

1. Facilitate attainment of regular cycles during the transition period from winter anestrus to the physiological breeding season. To facilitate attainment of regular cycles during the transition phase, mares should be examined to determine the degree of ovarian activity. Estrus in mares with inactive ovaries (no follicles greater than 20 mm in diameter) should be suppressed but these mares may not begin regular cycles following treatment. However, mares with active ovaries (follicles greater than 20 mm in diameter) frequently respond with regular post-treatment estrus cycles.

2. Facilitate management of the mare exhibiting prolonged estrus during the transition period. Estrus will be suppressed in mares exhibiting prolonged behavioral estrus either early or late during the transition period. Again, the post-treatment response depends on the level of ovarian activity. The mares with greater ovarian activity initiate regular estrus cycles and conceive sooner than the inactive mares. Regu-Mate® (altrenogest) Solution 0.22% may be administered early in the transition period to suppress estrus in mares with inactive ovaries to aid in the management of these mares or to mares later in the transition period with active ovaries to prepare and schedule the mare for breeding.

3. Permit scheduled breeding of mares during the physiological breeding season. To permit scheduled breeding, mares which are regularly cycling or which have active ovarian function should be given Regu-Mate® (altrenogest) Solution 0.22% daily for 15 consecutive days beginning 20 days before the date of the planned estrus. Ovulation will occur 5 to 7 days following the onset of estrus as expected for nontreated mares. Breeding should follow usual procedures for mares in estrus. Mares may be regulated and scheduled either individually or in groups.

DOSAGE CHART:		
Approximate Weight in Pounds	Dose in mL	
770	8	
880	9	
990	10	
1100	11	
1210	12	

ADDITIONAL INFORMATION: A 3-year well controlled reproductive safety study was conducted in 27 pregnant mares, and compared with 24 untreated control mares. Treated mares received 2 mL Regu-Mate® (altrenogest) Solution 0.22% (1.10 to body weight) 2x dosage recommended for estrus suppression from day 20 to day 322 of gestation. This study provided the following data:

- In filly offspring (all ages) of treated mares, clinical size was increased.
- Filly offspring from treated mares had shorter interval from Feb. 1 to first ovulation than fillies from their untreated mare counterparts.
- There were no significant differences in reproductive performance between treated and untreated animals (mares & their respective offspring) measuring the following parameters:
 - interval from Feb. 1 to first ovulation, in mares only
 - mean interovulatory interval from first to second cycle and second to third cycle, mares only
 - follicle size, mares only
 - at 50 days gestation, pregnancy rate in treated mares was 81.8% (9/11) and untreated mares was 100% (4/4)
 - after 3 cycles, 11/12 treated mares were pregnant (91.7%) and 4/4 untreated mares were pregnant (100%)
 - colt offspring of treated and control mares reached puberty at approximately the same age (82 & 84 weeks respectively)
 - stallion offspring from treated and control mares showed no differences in seminal volume, spermatozoal concentration, spermatozoal motility, and total sperm per ejaculate.
 - stallion offspring from treated and control mares showed no differences in sexual behavior.
 - testicular characteristics (scrotal width, testis weight, parenchymal weight, epididymal weight and height, testicular height, width & length) were the same between stallion offspring of treated and control mares.

REFERENCES:

Shoemaker, C.F., E.L. Squires, and R.K. Shideler. 1989. Safety of Altrenogest in Pregnant Mares and on Health and Development of Offspring. Eq. Vet. Sci. (9): No. 2: 69-72.

Shoemaker, E.L., R.K. Shideler, and A.O. McKinnon. 1989. Effects of Performance of Offspring from Mares Administered Altrenogest During Gestation. Eq. Vet. Sci. (9): No. 2: 73-76.

WARNING: Do not use in horses intended for food.

HUMAN WARNINGS: Skin contact must be avoided as Regu-Mate® (altrenogest) Solution 0.22% is readily absorbed through unbroken skin. Protective gloves must be worn by all persons handling this product. Pregnant women or women who suspect they are pregnant should not handle Regu-Mate® (altrenogest) Solution 0.22%. Women of child bearing age should exercise extreme caution when handling this product. Accidental absorption could lead to a disruption of the menstrual cycle or prolongation of pregnancy. Direct contact with the skin should therefore be avoided. Accidental spillage on the skin should be washed off immediately with soap and water.

INFORMATION FOR HANDLERS:

WARNING: Regu-Mate® (altrenogest) Solution 0.22% is readily absorbed by the skin. Skin contact must be avoided; protective gloves must be worn when handling this product.

Effects of Overexposure: There has been no human use of this specific product. The information contained in this section is extrapolated from data available on other products of the same pharmacological class that have been used in humans. Effects anticipated are due to the progestational activity of altrenogest. Acute effects after a single exposure are possible; however, continued daily exposure has the potential for more untoward effects such as disruption of the menstrual cycle, uterine or abdominal cramping, increased or decreased uterine bleeding, prolongation of pregnancy and headaches. The oil base may also cause complications if swallowed. In addition, the list of people who should not handle this product (see below) is based upon the known effects of progestins used in humans on a chronic basis.

PEOPLE WHO SHOULD NOT HANDLE THIS PRODUCT:

- Women who are or suspect they are pregnant.
- Anyone with thrombophlebitis or thromboembolic disorders or with a history of these events.
- Anyone with cerebral-vascular or coronary artery disease.
- Women with known or suspected carcinoma of the breast.
- People with known or suspected estrogen-dependent neoplasia.
- Women with undiagnosed vaginal bleeding.
- People with benign or malignant tumors which developed during the use of oral contraceptives or other estrogen-containing products.
- Anyone with liver dysfunction or disease.

ACCIDENTAL EXPOSURE: Altrenogest is readily absorbed from contact with the skin. In addition, this oil based product can penetrate porous gloves. Altrenogest should not penetrate intact rubber impervious gloves; however, if there is leakage (i.e., pinholes, spillage, no fit), or contaminated area covered by such occlusive materials may have increased absorption. The following measures are recommended in case of accidental exposure.

Eye Exposure: Immediately flush with plenty of water for 15 minutes. Get medical attention. **If swallowed:** Do not induce vomiting. Regu-Mate® (altrenogest) Solution 0.22% contains an oil. Call a physician. Vomiting should be supervised by a physician because of possible pulmonary damage via aspiration of the oil base. If possible, bring the container and labeling to the physician.

CAUTION: For oral use in horses only. Keep this and all medication out of the reach of children.

Store at or below 25°C (77°F).

NADA# 131-310, Approved by FDA.

HOW SUPPLIED:

Regu-Mate® (altrenogest) Solution 0.22% (2.2 mg/mL). Each mL contains 2.2 mg altrenogest in an oil solution. Available in 1000 mL plastic bottles.

* US Patents 3,453,267; 3,478,067; 3,484,462

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surveillance program of all breeding stallions in South Africa and determined that 1.35% of stallions (36 of 2,659) and 4.41% of exposed mares (three of 68) were positive on quantitative polymerase chain reaction testing, qPCR, a test that detects bacterial DNA.

May noted the reason the prevalence in exposed mares appeared higher than in stallions was that researchers only checked mares known to be associated with positive

stallions—a much smaller number than the total number of stallions checked. “If the entire mare population in South Africa was checked, then this percentage would be much lower,” May said. “This percentage did, however, confirm the importance of checking exposed mares during an outbreak situation, as a very small percentage may also become chronic carriers.”

It’s important that veterinarians in South Africa find the optimal test method

and swab sites for *Taylorella equigenitalis*. “South Africa is characterized by extensive distances, meaning that many of our practitioners are far away from approved testing centers, limited postal services, and periodic extremes of environmental temperatures,” May explained, which can prove challenging when culturing bacteria. “PCR therefore provided a practical, reliable, and sensitive method that facilitated the ability to detect *T. equigenitalis*.”

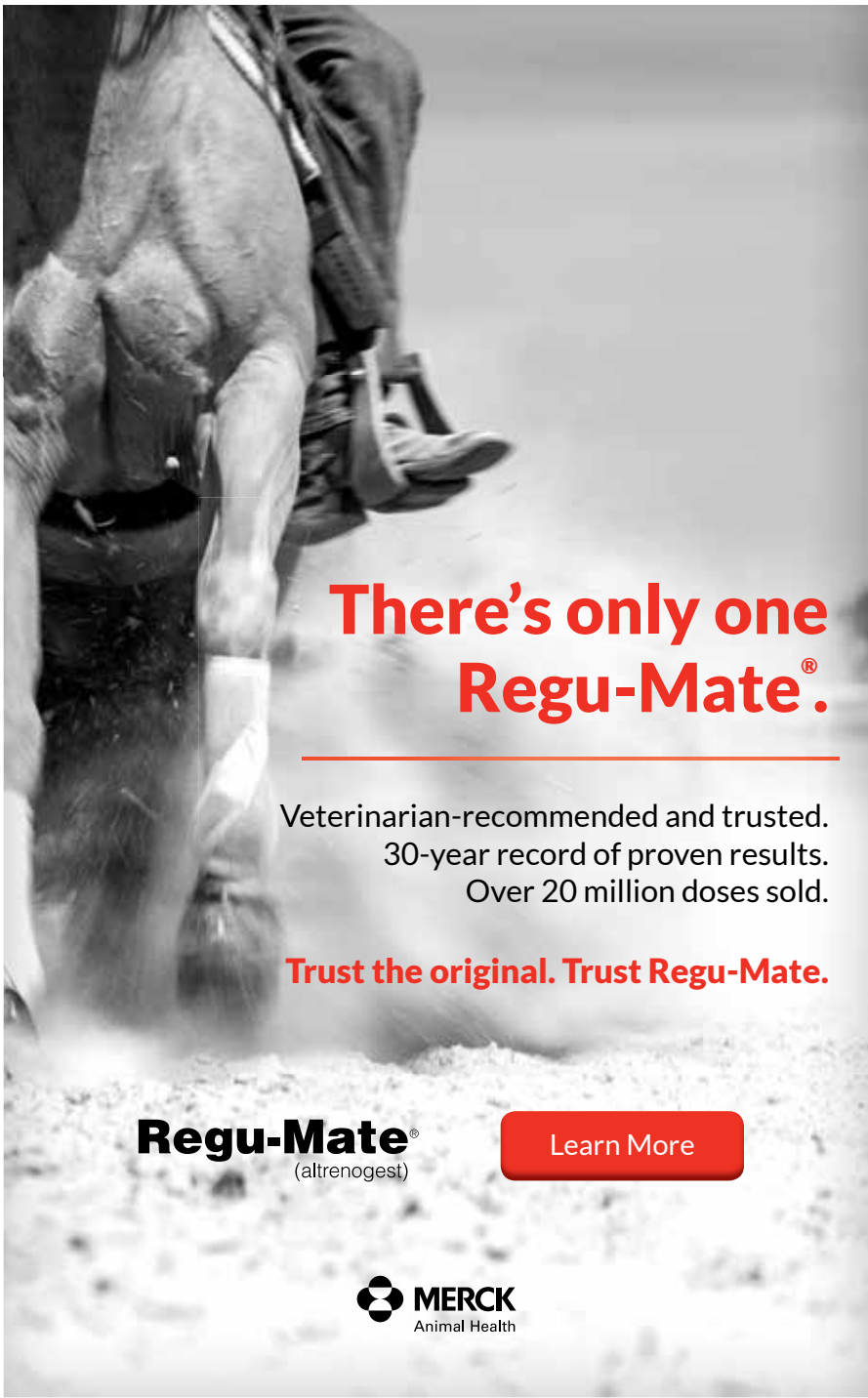
In regard to the optimal swab sites, “we hypothesized that there would be a single predominant predilection site for the organism in carrier stallions,” May said, noting that the researchers had assessed the frequency of the organism in the urethra (the membranous tube that transports urine out of the body), the urethral fossa (circular depression at the end of the glans penis from which the urethral process protrudes), and the lamina interna (the mucosa covering the penis, visible only when the penis is erect; in the relaxed state it telescopes inward from the preputial opening and lines the penis). In the 24 carrier stallions included in this study, the bacterial load in the urethral fossa was significantly higher than in the other two sites.

In conclusion, May said, “Although CEM is a fully treatable disease, the cost associated with an outbreak situation ... mean that a reliable and sensitive test and correct sampling techniques are of the utmost importance in rapid identification of the disease and to prevent the spread in a horse population.”

Accessory Sex Glands in Geldings

A gelding’s gonads are gone, but he’s still susceptible to problems developing in his reproductive tract, particularly abnormal growths in the accessory sex glands. When a gelding has signs of discomfort associated with the urogenital tract, it’s often difficult to determine whether the accessory sex glands are within normal limits of size and “character.” Researchers recently determined and described the ultrasound appearance of a group of “normal” geldings’ accessory sex glands so practitioners can better detect when something’s amiss.

Maria Schnobrich, VMD, Dipl. ACT, a reproduction specialist at Rood & Riddle, completed the research as a resident in the University of Pennsylvania School of Veterinary Medicine’s Department of Clinical Studies. The accessory sex glands (vesicular glands, prostate, ampullae, and



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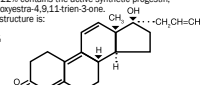


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DOSAGE AND ADMINISTRATION: While wearing protective gloves, remove shipping cap and seal; replace with enclosed plastic dispensing cap. Remove cover from bottle dispensing tip and connect luer lock syringe (without needle). Draw out appropriate volume of Regu-Mate solution. (Note: Do not remove syringe while bottle is inverted as spillage may result.) Detach syringe and administer solution orally at the rate of 1 mL per 110 pounds body weight (0.044 mg/kg) once daily for 15 consecutive days. Administer solution directly on the base of the mare's tongue or on the mare's usual grain ration. Replace cover on bottle dispensing tip to prevent leakage. Excessive use of a syringe may cause the syringe to stick; therefore, replace syringe as necessary.

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2. Facilitate management of the mare exhibiting prolonged estrus. Estrus will be suppressed in mares exhibiting prolonged behavioral estrus either early or late during the transition period. Again, the post-treatment response depends on the level of ovarian activity. The mares with greater ovarian activity initiate regular cycles and conceive sooner than the inactive mares. Regu-Mate® (altrenogest) Solution 0.22% may be administered early in the transition period to suppress estrus in mares with inactive ovaries to aid in the management of these mares or to mares later in the transition period with active ovaries to prepare and schedule the mare for breeding.

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DOSAGE CHART:

Approximate Weight	Dose
in lbs	in mL
770	7
880	8
990	9
1100	10
1210	11
1320	12

ADDITIONAL INFORMATION: A 3-year well controlled reproductive safety study was conducted in 27 pregnant mares, and compared with 24 untreated control mares. Treated mares received 2 mL Regu-Mate® (altrenogest) Solution 0.22% (110 lb body weight) (2x dosage recommended for estrus suppression) from day 20 to day 325 of gestation. This study provided the following data:

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- Filly offspring from treated mares had shorter interval from Feb. 1 to first ovulation than fillies from their untreated mare counterparts.
- There were no significant differences in reproductive performance between treated and untreated animals (mares & their respective offspring) measuring the following parameters:
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 - mean interval from first to second cycle and second to third cycle, mares only
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 - at 50 days gestation, pregnancy rate in treated mares was 81.8% (9/11) and untreated mares was 100% (4/4).
 - after 3 cycles, 11/12 treated mares were pregnant (91.7%) and 4/4 untreated mares were pregnant (100%).
 - offspring of treated and control mares reached puberty at approximately the same age (82 & 84 weeks respectively).
 - stallion offspring from treated and control mares showed no differences in seminal volume, spermatozoal concentration, spermatozoal motility, and total sperm per ejaculate.
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 - testicular characteristics (scrotal width, testis weight, parenchymal weight, epididymal weight and height, testicular height, width & length) were the same between stallion offspring of treated and control mares.

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Squires, E.L., R.K. Shideler, and A.O. Skinner. 1989. Reproductive Performance of Offspring from Mares Administered Altrenogest During Gestation. *Eq. Vet. Sci.* 9(1): No. 2: 73-76.

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HUMAN WARNINGS: Skin contact must be avoided as Regu-Mate® (altrenogest) Solution 0.22% is readily absorbed through unbroken skin. Protective gloves must be worn by all persons handling this product. Pregnant women or women who suspect they are pregnant should not handle Regu-Mate® (altrenogest) Solution 0.22%. Women of child bearing age should exercise extreme caution when handling this product. Accidental absorption could lead to a disruption of the menstrual cycle or prolongation of pregnancy. Direct contact with the skin should therefore be avoided. Accidental spillage on the skin should be washed off immediately with soap and water.

INFORMATION FOR HANDLERS: **WARNING:** Regu-Mate® (altrenogest) Solution 0.22% is readily absorbed by the skin. Skin contact must be avoided; protective gloves must be worn when handling this product.

Effects of Overexposure: There has been no human use of this specific product. The information contained in this section is extrapolated from data available on other products of the same pharmacological class that have been used in humans. Effects anticipated are due to the progestational activity of altrenogest. Acute effects after a single exposure are possible; however, continued daily exposure has the potential for more untoward effects such as disruption of the menstrual cycle, uterine or abdominal cramping, increased or decreased uterine bleeding, prolongation of pregnancy and headaches. The oil base may also cause complications if swallowed. In addition, the list of people who should not handle this product (see below) is based upon the known effects of progestins used in humans on a chronic basis.

PEOPLE WHO SHOULD NOT HANDLE THIS PRODUCT.

- Women who are or suspect they are pregnant.
- Anyone with thrombophlebitis or thromboembolic disorders or with a history of these events.
- Anyone with cerebral-vascular or coronary artery disease.
- Women with known or suspected carcinoma of the breast.
- People with known or suspected estrogen-dependent neoplasia.
- Women with undiagnosed vaginal bleeding.
- People with benign or malignant tumors which developed during the use of oral contraceptives or other estrogen-containing products.
- Anyone with liver dysfunction or disease.

ACCIDENTAL EXPOSURE: Altrenogest is readily absorbed from contact with the skin. In addition, this oil based product can penetrate porous gloves. Altrenogest should not penetrate intact rubber or impervious gloves; however, if there is leakage (i.e., pinholes, spills, etc.), the contaminated area covered by such occlusive materials may have increased absorption. The following measures are recommended in case of accidental exposure.

Skin Exposure: Wash immediately with soap and water.

Eyes Exposure: Immediately flush with plenty of water for 15 minutes. Get medical attention.

Ingestion: Do not induce vomiting. Regu-Mate® (altrenogest) Solution 0.22% contains an oil. Call a physician. Vomiting should be supervised by a physician because of possible pulmonary damage via aspiration of the oil base. If possible, bring the container and labeling to the physician.

CAUTION: For oral use in horses only. Keep this and all medication out of the reach of children.

Store at or below 25°C (77°F).

NADA# 131-310. Approved by FDA.

HOW SUPPLIED:

Regu-Mate® (altrenogest) Solution 0.22% (2.2 mg/mL). Each mL contains 2.2 mg altrenogest in an oil solution. Available in 1000 mL plastic bottles.

* US Patents 3,453,267; 3,478,067; 3,484,462

Manufactured by: DPT Laboratories, San Antonio, TX 78215

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ERICA LARSON



A gelding's gonads are gone, but he's still susceptible to problems developing in his reproductive tract, particularly abnormal growths in the accessory sex glands.

bulbourethral glands) are intimately associated with other organs (bladder, urethra, and ureters) and can be evaluated using transrectal ultrasound. Schnobrich and her PennVet colleagues used this approach in a group of 12 clinically normal light-breed geldings, ages 2-25 years old, with the goal of establishing a baseline for comparison. "This may help us in looking at geldings when we see them clinically," she said. Researchers had already characterized normal measurements of stallions' accessory sex glands ("These measurements come into play when we're doing breeding soundness exams, or evaluating stallions for pathology," but as far as she knew, these measurements weren't available for geldings, though she noted it is generally accepted that geldings' accessory sex glands are smaller than those of mature stallions.)

The team sought to obtain 24 separate measurements of the various components of the internal urogenital tract for each gelding. Some of their findings include:

- They identified a full complement of accessory glands in each animal and obtained 281/288 (97.6%) measurements.
- Schnobrich found both a 7.5 MHz linear-array transducer and a 6.0-10 MHz microconvex linear-array transducer, were effective and obtained similar measurements, but some structures (prostatic isthmus) were easier to identify using the microconvex transducer.
- Seminal vesicles are collapsible structures, making them difficult to image.
- Nine of 12 geldings had luminal contents

in the seminal vesicles with no clinical signs; six of those were "hypoechoic to anechoic," meaning the fluid appears dark to black on the ultrasound screen, and three of nine were "hyperechoic relative to the wall," meaning the contents were brighter or whiter than the seminal vesicle wall.

- The lumen of the ampullae was never larger than 1 mm, and seven of 12 subjects had hyperechoic luminal contents; four of 12 had hypoechoic contents. "The accessory glands are easily imaged in the gelding for one who is familiar with imaging these structures in stallions," Schnobrich said, "the only caveat being the prostatic isthmus is a little small. There was no difference between the size of the left and right side of the structures imaged, and both transducers worked equally well."

Veterinarians noting clinical signs such as blood in the urine or abnormal urination should consider prostatic abnormalities. These measurements might help them determine if there is a developing prostatic tumor or other pathology. Other potential problems associated with the accessory sex glands include seminal vesiculitis (inflammation of the vesicles).

"We conclude that the accessory sex glands can be reliably imaged in normal geldings," Schnobrich said. "We have successfully applied these values to the evaluation of geldings presenting to our hospital for clinical signs associated with the internal urogenital tract, thus demonstrating the utility of this data." 